Statement Regarding GHB (Xyrem) Approval

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My name is Joe Spillane. I am a pharmacist and a clinical toxicologist. I work as an associate professor at Nova Southeastern University College of Pharmacy and as a clinical coordinator at Broward General Medical Center in Fort Lauderdale, Florida. I also serve on the Broward County Commission on Substance Abuse and coauthor a twice-annual report on substance abuse trends in Broward County, Florida. I am not representing any organization and I have had no affiliation with Orphan Medical. I would like to voice some reservations that I have to the approval and scheduling of gamma hydroxybutyrate GHB (Xyrem) , but I would first like to mention the basis for my concerns.

I'd like to underscore the immense and rapidly growing popularity, highly addictive nature, and lethality of GHB and its precursors.

Overdoses & Drug Rape

In our emergency department alone, which treats approximately 70,000 patients per year, we had 48 GHB or GHB precursor overdoses in 1999. That number rose by approximately 60% to 77 cases in 2000. Most of these patients are brought in by rescue because of decreased level of responsiveness. All require monitoring and many require airway management including intubation and ventilation. Vomiting is particularly common with the abuse of this drug, which can have the potentially fatal consequence of aspiration in an individual with central nervous system depression. Most of our GHB abusers were young people (average age of 26.3yrs old) who were using the drug recreationally often while coingesting alcohol, ecstasy, cocaine, and/or marijuana.

We have had numerous patients say that someone must have given this drug to them without their knowledge, perhaps to facilitate robbery or sexual assault. There have been educational campaigns instructing people not to accept a drink from anyone but the bartender. However, we treated one of the local bartenders for GHB overdose recently who claimed that many of those employed in the local beverage industry are also using GHB and/or its precursors.

Withdrawal

We have treated 5 known cases of GHB or GHB precursor withdrawal in our facility. The sudden cessation of this drug results in physical withdrawal which is prolonged, impressive to observe, and very difficult to treat. Clinical manifestations of withdrawal have included tachycardia, sleeplessness, severe agitation, tremulousness, and hallucinations. Two of these patients experienced two separate withdrawal episodes. I submit that there are probably numerous other withdrawal cases at our institution and throughout the country that go unrecognized and are treated as psychosis.

Withdrawal is extremely difficult to treat and the long-term effects of multiple withdrawal episodes remains unclear.

Deaths

From 1996 through December 31, 2000, there have been nine fatalities in Broward County (a county of 1.6 million people) where GHB was considered one of the proximate causes of death. In most cases the drug was being used recreationally, in combination with alcohol and/or other central nervous system depressants. However, in July of 2000, a 25-yr. old white male was doing "capfuls of GHB all night long". Some friends left him briefly to rent a movie, and found him dead upon their return. On autopsy, his GHB level was very high, his alcohol level was zero, and no other drug was detected.

This is an important case to refute the common misperception that the drug is not lethal unless taken with other CNS depressants such as alcohol, and that the only treatment necessary for GHB toxicity alone is to "sleep it off".

Concerns

It is because of this experience in South Florida that I feel compelled to voice concerns over the scheduling and the proposed distribution system of Xyrem.

First, it is concerning to me that the entire system of distribution is voluntary and that there appears to be very little governmental/regulatory oversight. The proposed distribution system as I understand it, appears to be a fairly closed system where one pharmacy would store the drug and would be responsible for mailing the drug directly to customers. An exception to this would be made if third party payors insisted on the drug being sent to a pharmacy for dispensing. It certainly appears that the system is flexible and accommodating when profit margins might be affected. This is concerning because of the voluntary nature of the system and the understandable commitment of the company to maximize profits for their shareholders.

I also have concerns with the voluntary and proprietary nature of the data on GHB sales and distribution/diversion. Are there any guarantees of the availability of that data to governmental agencies? Again, it appears that all of this hinges upon voluntary action on the part of Orphan and the specialty pharmacy. What happens when the financial interests of the company conflict with the voluntary collection/submission of this information or indeed with the continuation of this closed loop system?

Given the addictive potential of this drug, I wonder what will happen to the patient who can no longer afford the medication or when the patient's insurance no longer covers this medication. What provisions would be made in these instances? What resources are available to treat the withdrawal? How will Orphan participate/contribute to those resources?

I think the potential for accidental pediatric poisoning should be addressed (and possibly already has been). This is a potentially lethal anesthetic/respiratory depressant that may be in a readily accessible container at a patient's bedside while they sleep.

Finally, deep and careful consideration should be given to the future impact of this "bifurcated scheduling" not just for GHB but for future medications. Couldn't any future manufacturer of an addictive/ or potentially abused medication claim that they designed a revolutionary system for distribution? Couldn't they then suggest it be made a schedule III or IV when used for "legitimate medical purposes" and schedule I when diverted? There would certainly be financial incentive on the part of the manufacturer to improve accessibility and cut the costs and potential obstacles of government regulation and oversight by doing so. Any future company could look confidently to the Xyrem decision as an applicable precedent.

Summary

In summary, I wanted to underscore the increasing abuse of GHB and its precursors, its use to facilitate sexual assault and robbery, its highly lethal and addictive properties, and its propensity to precipitate physical withdrawal. I strongly suggest that it would not be prudent to rely on a voluntarily closed system with very little regulation, very little oversight, and no guaranteed access to data to prevent its diversion. Further, the proposed bifurcated scheduling, while economically appealing to the manufacturer, is fraught with potential problems which could lead to increased diversion of GHB and a dangerous precedent for the future. I commend Orphan for their ingenuity and creativity, and for their commitment to bringing this medication to those who could benefit from it. Stricter control, with additional oversight, and verification would certainly enhance the possibility of attaining another one of Orphan's stated goals of reducing abuse and diversion. Thank you for a chance to participate in this important process.